Remarks

In accordance with the present invention, there are provided the crystal structure and atomic coordinates of a WW domain co-complexed with a WW domain binding agent. In addition, the invention provides methods of employing such crystal structure and atomic coordinates in methods of identifying WW domain binding agents. Also provided are crystalline WW domains, and crystalline complexes comprising a WW domain and a WW domain binding agent. The invention further provides computer programs for use in developing WW domain binding agents.

Claims 1-28 were pending prior to the present communication. Claims 17-28 have been withdrawn by the Examiner pursuant to Applicants' provisional election of Group I (claims 1-16; during a telephonic interview on June 6, 2003). Claims 1 and 13-16 have been amended herein to define Applicants' invention with greater particularity. These amendments add no new matter as they are fully supported by the specification and original claims. The present status of all claims in the application is provided in the listing of claims presented herein beginning on page 2.

The restriction of claims 1-28 under 35 U.S.C. § 121, as allegedly being drawn to three distinct inventions, is respectfully traversed. It is respectfully submitted that claims drawn to methods of identifying a WW domain binding agent based on computer modeling with a plurality of atomic coordinates obtained from a crystallized WW domain (Group I, claims 1-16) are intimately associated with claims drawn to computer programs for modeling atomic coordinates to define an interaction site of a WW domain (Group II, claims 17 and 18), and with claims drawn to WW domain crystals (Group III, claims 19-28). All three groups require the essential feature of a WW domain crystal, and thus, could readily be searched simultaneously without adding to the burden on the Examiner. A prior art search of methods of identifying binding agents using modeling of atomic coordinates of a crystal would, of necessity, involve a search of the crystal and computer methods of modeling of its atomic coordinates.

Therefore, no conservation of PTO resources would be realized if the restriction requirement into three Groups is maintained. Accordingly, reconsideration and withdrawal of the restriction requirement are respectfully requested.

However, in order to be fully responsive, Applicants affirm the provisional election of Group I (claims 1-16) with traverse.

The rejection of claims 1-16 under 35 U.S.C. § 103(a), as allegedly being unpatentable over Ranganathan *et al.*, *Cell* 89:875-886, 1997 (hereinafter referred to as "Ranganathan *et al.*"), in view of Verdecia *et al.*, *Nat. Struct. Biol.* 7:639-643, 2000 (hereinafter referred to as "Verdecia *et al.*"), and in further of U.S. Patent No. 6,495,376 issued to Lu *et al.* (hereinafter referred to "Lu *et al.*"), is respectfully traversed. Applicants respectfully submit that none of these references, either taken alone or in combination, teach or suggest the methods of claims 1-16. As acknowledged by the Examiner, "Ranganathan *et al.* do not disclose the contacting said potential binding agents in the presence of a WW domain substrate with the WW domain in order to determine binding preference (competition)" (see Office Action, Paper No. 13, at pages 4-5, bridging paragraph).

Thus, invention methods, as defined, for example, by claim 1, distinguish over Ranganathan *et al.* by requiring defining an interaction site of a WW domain based on a plurality of atomic coordinates, modeling a potential binding agent, and then contacting the potential binding agent with a WW domain in the presence of a WW domain substrate. Moreover, Applicants' invention, as defined by claim 1 as amended, further distinguishes over Ranganathan *et al.* by specifically referring to a plurality of atomic coordinates obtained from a WW domain crystallized in co-complex with a known WW domain binding agent, substrate, or inhibitor (supported by the specification, for example, at page 40, lines 27-29). Ranganathan *et al.* does not teach or suggest the recovery or use of information obtained from such a co-complex.

Applicants respectfully submit that Verdecia *et al.* is a publication (August, 2000) reflecting the inventors' own work disclosed within a year before the application filing date (December 8, 2000), and therefore cannot be used against the inventors of the present application as a 35 U.S.C. § 102 (or in turn 35 U.S.C. § 103) prior art document (*In re Katz*, 215 USPQ 14 (CCPA 1982); MPEP § 2132.01). Applicants are submitting herewith a Declaration under 37 C.F.R. § 1.132 establishing that the Verdecia *et al.* publication describes the work of Applicants Noel and Verdecia, and that the additional co-authors on this publication were merely conducting experiments under Applicants' direction and supervision. Therefore, Verdecia *et al.* is not available as a prior art reference, and thus, can not be used to overcome the deficiencies of the primary reference.

Moreover, Lu *et al.* is unable to overcome the deficiencies of the primary reference, because Lu does not teach or suggest the claimed methods. The present invention, as defined by claim 1, distinguishes over Lu *et al.* by requiring the modeling of a potential binding agent based on atomic coordinates obtained from crystals of a WW domain. Applicants' method relies on binding agents whose three-dimensional structures indicate they are likely to have robust interactions with a WW domain. In contrast, Lu *et al.* merely discloses the interaction of WW domain-containing polypeptides with ligands using only traditional binding assays (for example, incubating an uncharacterized test compound with a WW domain polypeptide). Furthermore, Lu *et al.* does not disclose either contacting a potential binding agent identified by modeling of atomic coordinates with a WW domain, or the determination or use of atomic coordinates obtained from a WW domain crystallized in co-complex with a known WW domain binding agent, substrate, or inhibitor.

Therefore, neither of the available prior art references (Ranganathan *et al.* and Lu *et al.*), either taken alone or in combination, teaches or discloses the claimed methods. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection of claims 1-16 under 35 U.S.C. § 103(a).

Conclusion

In view of the above amendments and remarks, prompt and favorable action on all claims is respectfully requested. In the event any matters remain to be resolved in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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Enclosure: Declaration under 37 C.F.R. § 1.132